

D4 a second Fab' fragment comprising the heavy chain variable region shown in Fig. 4B (upper) (SEQ ID NO. 3) and the light chain variable region shown in Fig. 4A (upper) (SEQ ID NO. 1)

wherein the first Fab' fragment specifically binds to the CD3 antigen and the second Fab' fragment specifically binds to the 28/32 kDa heterodimeric antigen on the surface of the malignant B cells ,

Remarks

New claim 43 recites a bispecific antibody comprising two Fab' fragments. The first Fab' fragment comprises the heavy and light chain sequences recited in claim 41. The second Fab' fragment comprises the heavy and light chain sequences of an exemplified form of humanized 1D10 antibody. Support for Fab' fragment is provided at *e.g.*, p. 23, line 20. Because claim 43 includes all the elements of claim 41, it is patentable for at least the same reasons.

Applicants respond using the paragraph numbering of the office action.

3. Copies of references said to be missing from the parent case are provided now.
4.
 - a. The cross-reference to related applications has been updated.
 - b. The title has been amended.
 - c. The handwritten lettering referred to by the Examiner was not intended to be part of the application.
5. It is believed that the requirement for a new sequence listing arises simply because of the unintended lettering of Figs. 5A and 5B noted above. As indicated this was not intended to be part of the application. Therefore, no additional SEQ. ID NOS are required, and the original sequence listing should suffice.

6. As noted, applicants are providing a clean copy of the figures without the unintended lettering.

7. Claim 41 has been amended as suggested.


9. Claim 40 has been amended as suggested.

10-12. Claim 42 has been canceled mooted the rejections.

13. Applicants provide a terminal disclaimer with respect to the parent patent US 6,129,914.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the title

The current title was deleted and replaced with –Humanized
Antibodies Against CD3--.

In the specification

The existing cross-reference to related application was deleted and
replaced with:

--The present application is a continuation of 08/397,411, filed March 1,
1995, now US 6,129,914, which is a continuation-in-part of 07/859,583, filed March 27,
1992, all incorporated by reference.--

In the claims

Claim 40 was amended as follows:

40. (Amended) The antibody of claim 39 wherein said position is
selected from the group consisting of H30, H67, H68, H70, H72 and H74.

Claim 41 was amended as follows:

41. (Amended) A humanized antibody that specifically binds to a
CD3 antigen on the surface of T cells, comprising a pair of humanized heavy chains and
humanized light chains, wherein the humanized light chain variable region comprises the
amino acid sequence of Fig. 5A (upper lines) (SEQ. ID. No. 8) and the humanized heavy
chain variable region comprises the amino acid sequence of Fig. 5B (upper lines) (SEQ.
ID. No. 10)

Claim 42 was canceled.

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The following new claim was added:

43. A bispecific antibody comprising;
- a first Fab' fragment comprising the humanized heavy chain variable region comprises the amino acid sequence of Fig. 5B (upper lines) (SEQ. ID. No. 10) and the humanized light chain variable region comprises the amino acid sequence of Fig. 5A (upper lines) (SEQ. ID. No. 8),
 - a second Fab' fragment comprising the heavy chain variable region shown in Fig. 4B (upper) (SEQ ID NO. 3) and the light chain variable region shown in Fig. 4A (upper) (SEQ ID NO. 1)
- wherein the first Fab' fragment specifically binds to the CD3 antigen and the second Fab' fragment specifically binds to the 28/32 kDa heterodimeric antigen on the surface of the malignant B cells.

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